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EXPERIMENTAL PATHOLOGY OF THE HIGHEST NERVOUS ACTIVITY

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Lecture delivered on May 10th, 1934 at the Post-Graduate Medical Institute in Leningrad

1935
State Publishing House
for Biological and Medical Literature
Leningrad Branch

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A few introductory words concerning the complicated fate of our work on the physiology and pathology of the highest nervous activity, accepting the fact that adjectives «highest nervous» correspond to the adjective «psychical», should first be stated.

Thirty-five years ago I was working on digestion — that was my former particular topic — and among other things I investigated the so-called «psychical secretion» of saliva. Intending to continue its analysis further, I soon came to the conclusion that if we take the psychological point of view and start to conjecture what the dog feels, thinks, etc. nothing would come of it nor could any precise knowledge be obtained. Then it was that I first decided to treat this psychical phenomenon, this «psychical saliva», just as objectively, just from without only, as is done with everything else studied in physiology. Soon there came forth an associate of mine Dr. I. F. Tolochinov and then we began this work together. With the help of numerous other assistants this work has been kept up without any breaks for the last thirty-five years.

The beginning of this work was marked by a slight though interesting event at our laboratory. When I de-

cided to carry the work on further, along those lines, one of my co-workers, a very clever, alert young man, engaged on another ordinary physiological topic, was very much astonished and even indignant at it. «How's this?» said he, «Good gracious! but to study the psychical activity on dogs, and in the laboratory!» And this, as it later appeared, proved very significant. Twelve years hence when I was in London attending the anniversary of the London Royal Society, I there met the most noted British neuro-physiologist C. S. Sherrington. «You know», he told me, «your conditioned reflexes could hardly be a success in England because they smell of materialism».

All right. Now, how do matters stand at present? It's necessary to tell you that those first impressions towards our new work still hold with a considerable section of the educated public; and it is due to this work that to many I am a very odious person.

Well, how about science? The situation, here too, is far from being definite. True, just as in that country wherein Sherrington tried to scare me, there has arisen an altogether different situation. Now, in England, the doctrine of the conditioned reflex is being taught in all schools. It has also received vast approval in the United States. But that, by far, is not the case everywhere. For example, the German approach to this doctrine is far from being such. Not so long ago, a German professor of physiology was visiting Kharkov. When he got to talking about the conditioned reflexes with the local professor of physiology, G. V. Volborth, one of my former assistants, he plainly announced that this was «keine Physiologie».

It should be added that in general, physiologists up to the present do not know the exact place that the conditioned reflexes hold in textbooks of physiology. To me it appears that by rights these reflexes should be placed foremost, when discussing the physiology of the cerebral hemispheres, as the normal objectively established work of these hemispheres. Analytic data which up to the present has been collected by means of stimulation, extirpation, and other methods of studying the cerebral cortex, should naturally be placed after the description of the normal activity.

I do not know what impression our up-to-date physiology of conditioned reflexes given you by Prof. N. A. Podkopaev has had upon you. While explaining the pathology of these reflexes, I dare take it into account that you have been convinced to what degree our method of treatment of the subject is expedient and fruitful. That is why I began with this short introduction.

Now I come to the subject itself. I am very glad that N. A. Podkopaev has given a course in the physiology of conditioned reflexes, before me, in this very hall, and thus I can avoid the necessity of giving you any preliminary explanations. I take it for granted that you all possess the fundamental physiological data and therefore shall proceed directly to the purely pathological matters.

Nervous activity, as all physicians know, consists of two mechanisms, of two processes: excitatory and inhibitory. Now with regard to these two processes, we distinguish three fundamental moments, namely, the force of these nervous processes, as excitatory and

also inhibitory; the mobility of these processes — inertness or lability, and finally, the equilibrium between these processes.

Certainly on the normal course of these processes, being of such nature, is based the whole of the highest nervous activity, by applying the usual terminology — psychical activity — not only of animals but also of man. At least, in the case of dogs — our usual experimental objects — we are gaining assurance that all their intricate and most complicated relations to their environment altogether come within the limits of our researches in the indicated processes and their nature. They are grasped by us to the extent that the possibilities of our experiments permit us.

All these processes with their basic habits, can be diverted from their usual tendencies and caused to become pathological. For this purpose we make use of strictly definite measures. There are three such measures: hypertension of the excitatory process, hypertension of the inhibitory process, and hypertension of the mobility of the nervous processes. With regard to the latter measure, it is necessary to state that it is practically the first time that I use the expression «hypertension of the mobility of the nervous processes». Usually this was known to us as a collision of the excitatory and inhibitory processes. In what manner is it possible to weaken the excitatory process and make it sick? For this purpose the nerve cell, within which the excitatory process is produced, should be acted upon by some external agent of great, unusual force; thus we overexert the work of the cell, overexert its excitatory process after which it becomes pathological.

In a similar manner, by hypertension, the inhibitory process can also be made pathological.

You already know how we produce inhibition by means of negative conditioned stimuli. Let us say that a given conditioned inhibitory stimulation has constantly aroused an inhibition, in its cell, for half a minute and that the cell has very well sustained it. Then I expressly prolong this same stimulus for five or ten minutes. A strong cell can sustain this, but in a weak cell the inhibition breaks down and the activity of the cell becomes pathological, transformed along different ways.

Finally, the third measure. We can arouse illness excitatory as well as inhibitory processes by means of changing quickly and without any intervals the state of inhibition in the cell into the state of excitation, or vice versa. This we usually consider as a collision in the excitatory and the inhibitory processes. It is clear that for any corresponding change in the activity of the cells in the cerebral hemisphere as for any other work, a certain time is required. When the collision is evoked, only those cells whose basic processes are strong and especially those with great lability may remain intact.

Now, what may happen as a result of the influence of those noxious measures? How is the deviation from the normal approached? How is the pathological state aroused in the cells? The cell generally becomes weakened. As regards the excitatory process, the cell becomes incapable of carrying on that work which it has hitherto performed, i. e., the limit of its working capacity is decreased and that becomes evident in the following pathological phenomena.

You already know that if we have before us a distinctly normal cell, and apply external agents of different physical strength as conditioned stimuli, then the conditioned effects of these stimuli keep more or less parallel with their physical strength.

Now, if I should cause that cell's break-down, i. e., overstrain it, it becomes ill. It arouses a different tendency of the cell to the stimuli. So the conditioned positive stimuli of different physical strength produce an equal effect and then we say that there exists the equalization phase of the cell's activity. Or, if the weakeness of the cell, i. e., the decrease of its limits of working capacity, progresses, there arises such a condition wherein strong stimuli produce a lesser effect than weaker ones. That is the paradoxical phase. Then finally a further disturbance of the cell's activity takes place thus; the cell now does not respond at all to the positive stimuli while inhibitive stimuli obtain a positive effect; we call this cell's state the ultraparadoxical phase.

Besides such decrease of the limits of working capacity, i. e., the weakening in the cell of the excitatory process one can also observe other changes of the excitatory process. The one that casts itself most before the eyes, particularly interesting and particularly applicable in neurology and psychiatry — is the inert state of the excitatory process, i. e., a state, when the excitatory process becomes obstinate, tenacious, much more slowly giving way to the inhibitive influences which arise normally.

I ought to linger a while on inertness. The excitatory process normally within us healthy people varies not only

in strength, but also in regard to its mobility. With some people the excitatory process is less mobile, with others more so, i. e., it yields sooner to stimulation, begins to react more quickly under the influence of stimulation; and thus, when the stimulation has acted and has ceased, the effect of the stimulation disappears sooner, more quickly than with another type of normal people.

On such basis we, like Hippocrates, divide the well balanced strong animals into two categories: the phlegmatic and the sanguinic. The phlegmatics will, consequently, be characterized by a relatively slow course of the excitatory process and the sanguinics otherwise.

But this is within the limits of normalcy. If I act upon the cell by our noxious methods I may make the inertness of its excitatory process become excessive and pathological so that the cell will immeasurably persist in its excited state.

Concerning the pathological changes of the excitatory process we must make an addition. Two morbid changes in its lability may be observed. I have just named you one of them. It is pathological stagnation. Under other morbid circumstances we can obtain an exact opposite state in the nerve cell — a pathological lability. That, in neurology, is termed excitatory weakness, i. e., the cell becomes very bustling, very rapid, responding to stimulation, and thus rapidly becoming bankrupt and weakening. We call this condition explosiveness.

In this same manner it is possible to break down, using our usual laboratory term, to make the inhibitory process pathological too. Suddenly but not gradually increasing the duration of the inhibitory state in a cell

very much through the influence of a respective external stimulus, we intensely weaken the cell's inhibitory function and almost completely destroy it. It must be stated, that in this respect the inhibitory process has been explored much less than the excitatory one.

Generally the inhibitory process also manifests itself in different ways with regard to its lability. It either develops quickly and finishes speedily or, on the contrary, it becomes more protracted. Therefore the inhibitory process may be either normally inert, or normally labile. However, it can also be driven into a pathological state with regard to inertness. At our laboratory we have one dog that has been displaying such pathological inertness for the last three years. In this dog under the influence of numerous collisions the positive stimulus began to evoke an inhibitory process instead of the normal excitatory one and so persistent was the process that though we constantly, for three years applied that stimulus, reenforcing it under favourable conditions, in no way could we restore him to his former positive effect. Only of late have we found means of changing those conditions: but I shall speak of that at the very end.

Thus you have before you, in general, the changes which arise under the influence of noxious agents, the change in the excitatory process, change in the inhibitory process and hence as a result, a disturbance of the regular relation between the excitatory and the inhibitory processes. But the normal activity of the nervous system is of course conditioned by a balance between those fundamental processes with their normal properties. One should tell you that it is often very easy to produce a

morbid state in the highest nervous activity by means of the above mentioned methods. But in the dependence of the types of the nervous system you could observe an enormous difference in the facility with which that morbid state can be attained.

In well balanced and strong animals, i. e., those in which both the excitatory and the inhibitory processes stand on the same level and whose mobility is also normal, it is certainly also possible to produce a nervous illness in them. But that takes considerable time and labour, because different means must be tried. In excitable and weak animals it is very easily attained. As you know, we call «excitable» that type in which there is a very strong excitatory process. The inhibitory process is probably also considerable but they do not correspond. The excitatory process strongly prevails, so much so, that in this type the negative stimuli almost never reach zero. Such a type may easily be «broken down», i. e., made pathological. If one offers it a series of problems wherein considerable inhibition is required, the inhibition becomes weak — the animal does not discern anything; further, it cannot inhibit anything, i., e. it becomes neurotic.

But in regard to the weak type, there by means of all our methods animals can very easily be made abnormal.

The neurotic state expresses itself by the fact that the animal does not properly respond to the conditions in which it is placed. This refers to laboratory characteristics as well as to its general conduct. Concerning the latter, everyone will agree that such a dog, having earlier been well, has since become ill.

At the laboratory we generally apply a system of positive and negative conditioned reflexes, elaborated on the basis of various unconditioned stimuli: positive reflexes to stimuli of different physical strength and different kinds of negative reflexes. This whole system is normally in accordance with strict rules: the positive effect depends upon the strength of the stimulus; the inhibitory stimulus gives a greatly decreased effect or none at all, etc. Under the influence of our noxious measures all or many of the normal reactions become weak and distorted.

The disturbed nervous equilibrium is clearly observed not only by us in the system of conditioned reflexes, but the servants also notice it. To them the dog was submissive. It has been trained to be orderly and knew where to go when led to experimentation. Now everything abruptly changed. The servants then simply say that the dog became stupid and had even gone mad.

The pictures of neurosis in animals that had become ill are sufficiently varied, due either to a different intensity of the illness or due to the appearence, in the foreground of either one or the other of the pathological symptoms. Latterly we have observed a very large number of those neuroses and neurotic symptoms on an organically morbid basis, i. e., on castrated animals. It is easily understood that castration itself violates the normal relations within the nervous system. Thus I shall devote a few words to describe the post-operative state of our dogs with regard to their nervous system.

One of the clearest neuropathological symptoms that appear almost immediately after castration is a great

decrease of the inhibitory process, of the inhibitory functions, so that a dog, that before castration had worked in an exemplary manner, in complete conformity with the conditions which had influenced its nervous system, has now become quite chaotic. Normally to-day, to-morrow, and the day after to-morrow, you see that the system of conditioned reflexes is absolutely uniform and thoroughly exact; while after castration no day is similar to another, a whole series of days each being different, there is not any order at all.

There is still another very important detail which appears shortly after the castration that has surprised even us. Talking of strong types, then their work, as I have just mentioned, after castration, becomes very much distorted instead of strictly regular, becomes chaotic. In weak types it is quite contrary: for some time after the operation that dogs behave better and more orderly than before. But true, this different condition exists only temporarily, for one, one-and-a half or two months. After that, of course, their nervous system also becomes weaker as in the strong ones. I shall later return to this question, on what it is based, and how this difference is understood by us.

After some time, after many months of entirely chaotic activity there appears a cyclic course in the work which had not existed before, i. e., the dogs work, manifest their system of conditioned reflexes not without interruption every day in a disorderly manner; but now their activity periodically changes. For some time it is chaotic and then for some time it spontaneously and markedly improves and becomes more orderly. The more time that elapses, the more clearly does that cyclic course

become manifest; thus the periods of better work are more frequent and prolonged, until after some years everything becomes normal. That evidently denotes some sort of adaptability in the organism.

Of course, since we are acquainted with the system of endocrine glands, which to a certain extent help and replace each other, it may be supposed that in the course of time that defect, which the organism bore immediately after the castration, is later more or less levelled out. But the restoration to the apparently normal after castration sets in at different periods in different dogs; with some it takes place after some months, with others after some years, while still other dogs have not yet reached that state. Evidently this is connected with the primary strength of the nervous system.

It is quite clear that in those castrates after their partial or total recovery different neurosis could be produced more easily than in quite normal dogs because they have already been made to lose their equilibrium and naturally are more fragile than normal dogs. Thus we may produce in them abundant different neurotic disturbances with the aid of the above noxious methods.

The morbid states of the nervous system, which we have produced, to a considerable extent correspond to the psychogenic illness in human beings. This same overstraining and these same collisions of the positive and inhibitory processes, all this can be met with in our own lives also. For example, someone has insulted me deeply and for some reason I have been unable to reply by corresponding words or especially by actions and thus had to overcome this struggle or conflict of the excitatory and the inhibitory processes within myself; and that has been

repeated not only once. Or let's take a case from the literature of neuroses: a daughter is present at the last days and hours of her dearly beloved father. She must put on an appearance as if everything were all right and that everybody expects him to recover, while she is actually weighed down by mortal anxiety and grief. This frequently leads to a break-down and to a neuroses.

And really, wherein should the actual difference physiologically be between such break-downs and the case wherein the excitatory and the inhibitory processes in our experimental animals are allowed to collide?

Moreover, besides such neuroses, as a result of the extremely complicated make up of our brain as compared with the higher animals, there must also be special human neuroses. I ascribe psychasthenia and hysteria to the latter. These cannot be produced in dogs. Because in such cases it is taken into consideration that the human brain is divided into a higher — a purely human part, connected with speech — and a lower part which, just as in animals, receives the external impressions and directly analyses and synthesises them in a certain manner. Still, neurasthenic conditions of various kinds can plainly be produced in animals.

Because our materials appeared to me to be sufficient for the purpose of physiologically understanding the mechanisms of nervous diseases, I began to visit, two or three years ago, the neurological and the psychiatric clinics (of course without devoting a great deal of time). I can say with regard to the neurological clinic that nearly all the neurotic symptoms and pictures observed there could be understood and connected with our pathophy-

siological laboratory findings. And this is not only my opinion, the opinion of a physiologist, but is also the opinion of the neuropathologists who have been acquainting me with the clinic, and who agree that our physiological understanding of neuroses is not phantastic; that we are really laying a sound foundation for a constant contact between our laboratory facts and the human neuropathological phenomena.

Before proceeding to another category of our facts I shall explain one of the above-mentioned phenomena which has remained without any further analysis.

Why is it that after castration animals with a strong nervous system directly become chaotic, and only later their conduct in course of time, levels out more or less, while animals with a weak nervous system, on the contrary, immediately after castration behave better, and in a more regular manner than before the operation, and only later become invalids?

We feel that this is the best way to explain it. An animal experiences sexual stimulation when the sex glands are normal; consequently additional impulses move towards the brain and tonify it; but the brain is weak. Hence the deficiency in the general nervous activity. With the removal of those glands the additional stimuli drop off, the nervous system is eased, and its work becomes in other respects more expedient. This is not a phantastic explanation. We know exactly the same in another more tangible case. If we take a dog in one or another degree of appetite, it is of great significance in our system of conditioned reflexes. If you have before you a strong dog and you increase its food excitability in some way or another (while experimenting with food reflexes),

then all its conditioned effects are increased. With a weak type it is the contrary: an increased food exitability generally causes the conditioned reflexes to diminish, i. e. for it such additional excitation is insupportable and is accompanied by inhibition which therefore we term protective.

Now, I shall turn to another category of facts. The fact that by means of definite methods we produce definite morbid states of the nervous system of course is based upon this circumstance that our conception of the mechanism of that system is correct to a certain degree. Of course, the power of our knowledge with regard to the nervous system will be apparent to a still greater degree if we could not only injure the nervous system, but also repair it afterwards, according to our wishes. Then it will be definitely proved that we have mastered those processes and are able to control them. That is just so; in many cases we not only produce an illness, but we remove it, so to say by order, altogether accurately. Of course, in this case, before all else, instead of guessing and applying various means at random, we should make use of the indications which medicine gives us. Bromides thus play a great rôle with us. But in order to operate with this drug accurately it was necessary to know the mechanism of its action thoroughly.

With regard to bromides we have definitely fixed the fact—without the least doubt—that their action is not at all such as has been hitherto supposed and possibly is still considered thus by pharmacologists. Their physiological effect does not consist in a decrease of the excitability or in the weakening of the excitatory process, but in the reinforcement of the inhibitory process. Bromides have

a special relation to the inhibitory process and that can be shown by many different experiments. Here, for example, is the simplest experiment which we usually apply in case of an emergency.

You have an excitable type of dog — that type whose excitatory process is excessively strong and whose inhibitory process is relatively weak, and consequently the dog cannot lead its inhibitory reflexes to a complete zero. It has insufficient inhibition. You give the dog a bromide and immediately get complete inhibition. You frequently receive in such cases a greater positive effect than previously, before the bromide was administered. However, there is another side to the effect of bromides which is no less important.

Though bromides — and rightly — have been in use as a nerve drug for many years (I do not know exactly how many, but not less than 60—70 years) — however, the absolute truth is that until recently medicine has not always used this mighty therapeutic nerve instrument, bromides properly. In this way it was responsible for many a serious mistake.

You administer bromide in a case of a neurotic state. Suppose the bromide has no effect. Then you augment the dose thinking that too little was given before. But that is right only in one series of cases. In other cases, and probably in the majority, you must decrease the dose and not augment it. And often you must vastly decrease the dose. The gradation of the useful doses of bromides is enormous; in our dogs its limits are approximated to a thousandfold. That is absolutely correct and we all guarantee it. Consequently in medicine, in this respect, a serious correction

should be made. If you administer an incongruously great dose and obtain harmful instead of beneficial results, you may seriously injure the patient.

Of course, there can be no question that this is true with dogs, but with nervous people matters are quite different. The neurologists in our clinics have already observed that when they took into consideration these facts it became evident that in many cases, for success in treatment, it was very necessary to decrease the doses of bromides, down to decigrams and centigrams per dose, but not to increase it. The general laboratory rule is: the weaker the type of nervous system and the given nervous state, then the smaller must the dose of bromide be.

A known curative effect in laboratory neuroses appertains to rest also, as is well known in medicine. If you have made a dog neurotic, it often may be helped by not working with it every day, because a daily system of our conditioned reflexes undoubtedly is a difficult problem wherein such a state is impossible for the dog. It would be well for you to have a regular 2—3 day recess between experiments and the nervous system will recover.

In some cases it has been observed that rest, as it were, takes the place of bromides. Suppose you have a dog which works in a chaotic manner after castration. You can help it in two ways: either by making it work, i. e., you experiment with it not every day, but with rest periods of 2—3 days, and thus it already will to a considerable degree work better, or else a suitable dose of bromide will produce the same results.

I must say that of late there came to us still another extremely important manner of treatment, but as yet we have no authority to speak definitely of it as an agent of radical treatment. However, it is impossible to pay no attention to and not to look upon it with great hope.

By means of our noxious measures with which the whole cerebral cortex is made pathological it is also possible to cause an entirely isolated area of the cortex to become ill; this is an extremely important and very impressive fact.

Suppose we have a dog with a series of different conditioned acoustic stimuli: beats of the metronome, a noise, a tone, a crackling and a gurgling sound, etc. It is easy to obtain of all these stimuli only one which would be harmful and would produce a sharp deviation from normalcy. While you apply the other acoustic stimuli the animal keeps and works in good order quite regularly; but as soon as you touch upon the point which is related to this noxious stimulus, not only the reaction on it will be in that manner or otherwise distorted, but after that the whole system of conditioned reflexes will be disturbed and the harm of it will spread over the whole cerebral cortex. This fact itself leaves no room for doubt because many scientific workers have frequently produced and are producing that phenomenon.

Here I want to draw your attention to the following. When I enumerated for you all our sounds it was clear that they were more or less complex. How can we present to ourselves an illness of the cerebral cortex with regard to separate sounds? Scarcely can it be

supposed that for each sound that we apply there corresponds a particular group of nerve cells which receive elementary acoustic stimuli, of which our sound consists. It is more probable that in the case of each of our sound stimuli, it is a question of a dynamic structural complex, the elements of which, the corresponding cells, take part in other dynamic complexes also, when other composite sounds are used. In the processes which connect and systematize the dynamic complexes, our noxious methods create difficulties, the results of which are the basis for disturbances and destructions in those complexes.

Isolated morbid points can be obtained in all parts of the cerebral hemispheres. Take the following case. You elaborate conditioned positive stimuli from a mechanical stimulation of the skin in different parts of the body. It can be done so that the excitatory processes at two points of the skin will be all right, while the third point will be functionally ill.

We now have a dog belonging to the excitatory type, i. e., one in which the excitatory process is extremely strong but with insufficient corresponding inhibition. It was castrated. Being a strong type it got well quickly enough. Since it was excitable, much time and labour had to be spent, before the castration, in order to elaborate a differentiation to the metronome. During the period after its castration due to some difficulties at the laboratory there was a scarcity of animals' food and they became considerably worn out. On the basis of a general exhaustion of the nervous system our dog's reflex to the metronome which had been complicated by its difficult differentiation, became morbid,

while all the other conditioned reflexes remained intact. As soon as metronomes were used, the normal work with conditioned reflexes became impossible. We tried not to make use of the inhibitory metronome as it was the more difficult one, but used the positive one only. But that did not change the situation. Bromides proved to be ineffective in general, for some unknown reason, in cases of illnesses of isolated points in the cerebral hemispheres.

Then before us the question arose: will not the same be the case in another region, in another analyser of the cerebral hemispheres where the excitatory and the inhibitory processes would collide? For this purpose the skin area was selected, because to it we could apply an easier differentiation, namely one spot of the skin was made positive and another inhibitory; the stimulation of one spot was reinforced by feeding, while the other was not. The results were the same. While only the positive conditioned stimulus was being elaborated, the dog behaved quite normally and the whole system of reflexes was in order. However, as soon as the inhibitory stimulus began to appear, all the reflexes diminished, were distorted, and the dog became so violently furious, that the experimenter could not stick the apparatus to the skin or take them off without danger of being bitten.

Now I shall draw your attention to the following interesting thing. When in other dogs we had such morbid isolated points in the cortex, their harmfulness, their illness was only expressed by the fact that their stimulation led to a disturbance or even to a destruction of all our system, but we never found that this was accompanied by an expression of ordinary pain in the

animals. Now, here then was a distinct impression as if a touch of the skin turned into pain. How can that be understood?

In reality the only difficulties during a collision of the excitatory and the inhibitory processes which were noted in the system of conditioned reflexes were in the brain. Where then did the pain of the skin come from? Evidently this may and should be explained in the following manner. In this dog in the cerebral cortex at a certain point there takes place a great hardship, which ought to be painfully felt, just as you feel when you are solving an extraordinarily difficult problem. You feel a certain heaviness in your head, which is an extremely disagreeable feeling. We must also admit a similar condition in our dog. But in the course of all those experiments it has apparently formed a conditioned connection between the sticking on of the apparatus to the skin and the difficult state of the skin analyser in the brain. By conditioning it transfers the struggle against the difficult state in its brain to the moment when the skin is stimulated and thus manifests a struggle against any contact with the skin. However, that is not a hyperaesthesia of the skin. Thus this is a very interesting case of an objectivation of an internal cerebral process, a manifestation of the strength of its connection with skin-stimulation; while in the brain we may expect simply a special kind of heavy sensation like a peculiar pain. It wasn't in vain that psychiatrists have termed melancholia a psychical pain, namely a cortical pain, characterized by the sensation which differs from the pain inflicted by wounds or diseases in different parts of the organism.

Thus, with this dog, for a long time we could do nothing. At last a favourable outlet appeared due to the good fortune of one of my most valuable co-workers of long standing Dr. M. K. Petrova. She formerly was a therapist and later was enticed into the conditioned reflex field. Now for many years she has devoted herself entirely to it. In connection with this an interesting thing happened to me. I must say that though I began my professorship as a pharmacologist, I have always had a strong prejudice against introducing several substances at one time into the organism. It always seemed strange to me when I saw a prescription with 3 or more drugs in it. What a dark mess this would be! Thus much more so was I always against such combinations of pharmacological substances in physiological analyses of phenomena, because my point of view was that the simpler the conditions of phenomena, the more chances are there for deciphering them. I had permitted bromides to our laboratory as a single drug on the basis of medical practice; caffein was also introduced for separate use as a stimulant bearing on the excitatory process; but I was very much against combining them. However, the therapist, being generally accustomed to combinations, insisted upon a trial and proved to be right. The result was extraordinary, wonderful! When a mixture of bromide and caffein was administered to the above-mentioned dog, all at once not a trace of that tenacious neurosis was left. We acted carefully. Administering that mixture of caffein and bromide for two days, we at first tried only the positive mechanical stimulation of the skin. The effect proved to be normal. The animal remained absolutely quiet, there

being no depravation of the system of conditioned reflexes. A little later, being encouraged by the results on the positive stimulus, we applied the negative one. Here too, the same thing happened; there was not the least hint of the former morbid reaction.

Post factum it was easy for me to construct a corresponding theory. I presented the case to myself as follows: certainly it must be understood that in most cases, in diseases of the nervous system, there is a disturbance of the correct interrelations between the excitatory and inhibitory processes, as it appeared when applying our noxious methods. Now if we have, let us say, two levers in the form of pharmaceutic drugs, two communicators towards the two chief apparatus, namely the two processes of the nervous activity, then put into action and correspondingly change the force of one or the other lever, we have a chance of restoring the disturbed processes in their former place, into their correct interrelations.

We also have another similar case. I have already mentioned a dog whose pathological inertness of the inhibitory process has lasted for three years, i. e., its positive process has become ill, the positive stimulus has turned into an inhibitory one. Though we have constantly been reinforcing this stimulus, i. e., we fulfilled those conditions under which it ought to be positive, for a full 3 years we have had it constantly inhibitory. What didn't we try out, bromides, rest, etc. — but nothing helped! Under the influence of a mixture of bromide and caffein, that stimulus which for such a long time gave a morbid reaction now has attained a normal positive effect.

In that same dog, parallel with that pathological inertness of the inhibitory process, a pathological lability of the excitatory process existed on another stimulus, i. e., it developed its action not gradually but impetuously, in an explosive manner. But still during that excitation already there was quickly aroused a negative phase. At the first moment, at the application of this conditioned stimulus, the dog violently strove to the feeder and there was abundant salivation; but then soon after, still during the time of excitation, the salivation stopped. When you began to reinforce the stimulus, offered food, the dog would not take it and turned away. This pathological phenomenon under the influence of our mixture also disappeared, and the morbid stimulus had become normal in its action.

Further, the following is certainly interesting. After having applied our mixture to this dog for ten days we decided to find out whether that cure were radical. It appeared to be not so. After we had ceased to administer our mixture, the former relations returned. Of course, it may be that much more time is necessary to set the disturbance entirely right. But another idea is also possible: we really establish correct interrelations between both processes changing them temporarily, but we do not treat those processes themselves or at least both of them together. Clearly, if it is the first case, then it is a great triumph of therapy. In any case, during the present palliative treatment and possibly a future radical one, in a mixture of bromide and caffein, we must take into consideration the extreme exactness of the doses of both medicines, reducing, especially with the caffein, even to milligrams.

In conclusion I wish to stop awhile on the problem of the transfer of our laboratory results to the neuropathological and psychiatric clinics. As regards the first, it cannot be doubted that our human neuroses can be understood altogether satisfactorily in the light of our laboratory analysis. Some things, it seems to me, are also being cleared up in psychiatry due to our laboratory findings.

At present I am publishing some pamphlets headed: «Latest Communications on the Physiology and Pathology of the Highest Nervous Activity». Two articles of the last publication have been translated into foreign languages. One has been published in French [1], the other has been sent to an English psychiatric journal [2], and I am interested, as can be understood, to know the reaction of our and foreign specialists.

You are aware now that at the laboratory we can make ill separate points of the cerebral cortex of an animal by functional means, while all the rest remains fully sound. I want to make use of this fact of isolated illness in order to understand a very interesting and enigmatic psychiatric form, namely paranoia. The latter, as is known, is characterized by the fact that an intellectually healthy person, who takes logic and reality into account as all healthy people do, a person who may even be gifted, as soon as one certain subject is mentioned he becomes clearly psychotic. He now does not acknowledge any logic or reality. It seems to me that this form can be

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[1] Journal de Psychologie normale et pathologique. XXX[e] Année, Nos. 9—10.

[2] The Journal of Mental Science, April, 1934.

understood on the basis of our laboratory results concerning isolated illness of separate points in the cerebral cortex.

It can scarcely be disputed that stereotype skeletal movements may and should be understood as expressions of a pathological inertness of the excitatory process in the cortical cells which are connected with movement. That perseverations should be looked upon in this same manner only in the cells of speech movement. But at first glance it is more difficult to explain in the same manner fixed ideas and paranoia. However, understanding isolated morbid points of the cortex not only in a literally crude anatomical sense but also in a structurally-dynamic one (as I have mentioned above) seems to me, has set aside this difficulty to a sufficient degree.

Here is another case: it seems to hover between neurosis and psychosis. In cases of persecutory delusions sometimes the patient irresistibly considers reality that which he fears and wants to avoid. For instance, he desires to possess a secret and it appears to him that all his secrets are constantly being disclosed in some way. He wants to be alone, even though he is alone in his room and everything lies open before his eyes, he still imagines that someone else is there with him. He wishes to be respected and it seems to him that literally at every moment he is being insulted in some way or other by words, signs, or facial expressions. Pierre Janet calls it «les sentiments d'emprise», as if someone is taking hold of the patient.

It seems to me that this case physiologically is based upon the ultraparadoxical phase, which I have already mentioned and which you know consists of the following.

Take the case when two metronomes of different frequency act as conditioned stimuli: the one with 200 beats per minute is the positive stimulus and the other with 50 beats — the negative one. Now, if the nerve cell develops a morbid state or simply a hypnotic state, the reverse effect can be noted: the positive stimulus becomes inhibitory and the inhibitory becomes positive. This is a perfectly exact laboratory phenomenon and one that constantly takes place. Now I understand the patient's state thus. When he desired to be alone or to be esteemed, this then is a strong positive stimulus which provoked in him the exact opposite conception involuntarily and irresistibly according to the ultraparadoxical rule.

Thus you see that in the field of pathology our method of work, the method of objective treatment of the highest phenomena of the nervous activity, is entirely justifiable for animals; the more we apply it, the more is it justified. At present we are making, as it seems to me, warrantable attempts to apply that very method even to the highest nervous activity in man which is generally called the psychical activity.

That is all that I wanted to tell you.

Printed in the Second Printing Office „Pechatny Dvor" of the Trust „Polygraphkniga", Leningrad.

Цена 45 к.